C/EBP-mediated transcriptional mechanisms in mononuclear phagocytes.

L1 ANSWER 90 OF 3427 CAPLUS COPYRIGHT 2005 ACS on STN
2005:417501 Document No. 142:424484 Quantitative two-step RT-PCR for the detection of human ABCA1 transporter on LightCycler using hybridization probes and external standards. Kielar, Danuta; Dietmaier, Wolfgang; Langmann, Thomas; Aslanidis, Charalagmpos; Probst, Mario; Naruszewicz, Marek; Schmitz, Gerd (Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, 93042, Germany). Rapid Cycle Real-Time PCR: Methods and Applications--Genetics and Oncology, 15-25. Editor(s): Dietmaier, Wolfgang; Wittwer, Carl; Sivasubramanian, Natarajan. Springer-Verlag: Berlin, Germany. ISBN: 3-540-42600-0 (English) 2002. CODEN: 69DCR7.
AB Authors describe here a real-time RT-PCR method for detection and quantification of minute amts. of ABCA1 mRNA. ABCA! transcripts were quantified in various human tissues, as well as in monocytes, macrophages, **THP-1** cells, fibroblasts, adipocytes, preadipocytes, keratinocytes and in Hela cells transfected with SP1 and Sp3 transcription factors.

10/716652

```
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      8349376 1
L2       4148 MCP-1
               (MCP(W)1)

=> d his

     (FILE 'HOME' ENTERED AT 09:33:20 ON 03 AUG 2005)

     FILE 'CAPLUS' ENTERED AT 09:33:32 ON 03 AUG 2005
L1        3427 S THP-1
L2        4148 S MCP-1

=> s l1 and l2
L3         140 L1 AND L2

=> d 1 2 3 5 10 20 30 40 50 60 70 80 100 120 130 140 cbib abs
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L3 ANSWER 1 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN
2005:647710 Kinetic analysis of cytokine response to cigarette smoke condensate by human endothelial and monocytic cells. Nordskog, Brian K.; Fields, Wanda R.; Hellmann, Gary M. (Department of Physiology and Pharmacology, Wake Forest University School of Medicine, Medical Center Blvd., Winston-Salem, NC, 27157-1083, USA). Toxicology, 212(2-3), 87-97 (English) 2005. CODEN: TXCYAC. ISSN: 0300-483X. Publisher: Elsevier B.V..
AB Atherosclerosis is generally considered an inflammatory disease characterized by the accumulation of lipid in large and medium elastic arteries. Individuals who smoke are at increased risk for developing atherosclerosis and the clin. events associated with this disease. Underlying the mechanisms involved in atherosclerotic lesion development exists a complex pattern of signaling, involving mols. (cytokines and chemokines) that mediate the progression of arterial lesions. The unique nature of exposure to tobacco-related toxicants during the process of smoking prompted our investigation of the time-dependent responses of two critical cell types to cigarette smoke condensate exposure. In this study, we examined the kinetic responses, using suspension array technol. and RT-PCR of 17 cytokines (IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-17 GM-CSF, G-CSF, INF-γ, TNF-α, **MCP-1** and MIP-1β) in human aortic endothelial cells (HAECs) and **THP-1** monocyte macrophages following exposure to cigarette smoke condensate (CSC) for 24 h. In HAECs, IL-8 and

IL-4 were rapidly stimulated by CSC exposure while, surprisingly, **MCP-1** expression was downregulated. In **THP-1** macrophages, IL-6, MIP-1β, **MCP-1** and IL-1β protein expression were suppressed upon CSC exposure. All other measurable cytokines in **THP-1** cells exposed to CSC had levels of protein and mRNA similar to controls. Depending on cell type, CSC uniquely influences the expression of cytokines. The complex interplay of these signaling mols. within the framework of atherosclerosis points to the ability of cigarette smoke components to alter such signaling following acute exposure, and by this mechanism may alter the course of both atherogenesis initiation and progression.

L3 ANSWER 2 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

2005:647340 Involvement of Arp2/3 complex in **MCP-1**-induced chemotaxis. Mukai, Yasuo; Iwaya, Keiichi; Ogawa, Hitoshi; Mukai, Kiyoshi (Department of Diagnostic Pathology, Tokyo Medical University, Tokyo, Japan). Biochemical and Biophysical Research Communications, 334(2), 395-402 (English) 2005. CODEN: BBRCA9. ISSN: 0006-291X. Publisher: Elsevier.

AB The migrating monocyte shows dynamic actin polymerization in response to **MCP-1**. We investigated the involvement of the actin-related protein 2 and 3 complex (Arp2/3 complex) during chemotaxis of a human monocyte cell line (**THP-1**). To clarify whether the Arp2/3 complex directly polymerizes actin in response to **MCP-1** stimulation, **THP-1** cells were transfected with complementary DNA constructs encoding ScarWA. In ScarWA-transfected cells, neither recruitment of Arp2/3 complex at the leading edge nor actin polymerization was detected. Indeed, migration induced by **MCP-1** was almost completely blocked. At the same time, transfection also interfered with the recruitment of integrin β-1 at the leading edge and reduced affinity binding to fibronectin. Immunopptn. with an anti-Arp2 antibody showed that integrin β-1 and WASP were co-precipitated under the condition of **MCP-1** stimulation. These results indicate that interaction between the Arp2/3 complex and WASP stimulates actin polymerization and integrin β-1-mediated adhesion during **MCP-1**-induced chemotaxis of **THP-1** cells.

L3 ANSWER 3 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

2005:624075 Effect of montelukast on nuclear factor κB activation and proinflammatory molecules. Maeba, Shinji; Ichiyama, Takashi; Ueno, Yoshiko; Makata, Haruyuki; Matsubara, Tomoyo; Furukawa, Susumu (Department of Pediatrics, Yamaguchi University School of Medicine, Yamaguchi, Japan). Annals of Allergy, Asthma, & Immunology, 94(6), 670-674 (English) 2005. CODEN: ALAIF6. ISSN: 1081-1206. Publisher: American College of Allergy, Asthma, & Immunology.

AB Background: Montelukast is known as a cysteinyl leukotriene 1 receptor antagonist. However, the action of montelukast in terms of nuclear factor κB (NF-κB) activation and the production of proinflammatory mols. is unknown. Objective: To demonstrate the potential anti-inflammatory effect of montelukast. Methods: We examined whether montelukast inhibits the activation of NF-κB, a transcription factor that regulates the expression of proinflammatory mols. The inhibitory effects of montelukast on tumor necrosis factor α (TNF-α)-induced NF-κB activation on **THP-1** cells, a human monocytic leukemia cell line, were evaluated by flow cytometry, and those on lipopolysaccharide-induced interleukin 1β (IL-1β), IL-6, TNF-α, and monocyte chemoattractant protein 1 ( **MCP-1**) production in peripheral blood mononuclear cells were evaluated by ELISA. Results: Flow cytometry demonstrated that montelukast inhibited NF-κB activation in **THP-1** cells in a dose-related manner. Furthermore, 10-5M montelukast significantly inhibited lipopolysaccharide-induced IL-6, TNF-α, and **MCP-**

1 production in the peripheral blood mononuclear cells of controls and patients with asthma. Lipopolysaccharide-induced IL-1β production was not inhibited by montelukast. Conclusions: These findings suggest that high doses of montelukast modulate the production of IL-6, TNF-α, and **MCP-1** through the inhibition of NF-κB activation. However, the anti-inflammatory effect of montelukast at therapeutic doses in patients with asthma needs to be further investigated.

L3 ANSWER 5 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN
2005:344049 Document No. 142:479831 Shear Stress Inhibits Smooth Muscle Cell-Induced Inflammatory Gene Expression in Endothelial Cells. Chiu, Jeng-Jiann; Chen, Li-Jing; Chang, Shun-Fu; Lee, Pei-Ling; Lee, Chih-I.; Tsai, Min-Chien; Lee, Ding-Yu; Hsieh, Hsing-Pang; Usami, Shunichi; Chien, Shu (Division of Medical Engineering Research, National Health Research Institutes, Miaoli, Taichung, Taiwan). Arteriosclerosis, Thrombosis, and Vascular Biology, 25(5), 963-969 (English) 2005. CODEN: ATVBFA. ISSN: 1079-5642. Publisher: Lippincott Williams & Wilkins.
AB Vascular endothelial cells (ECs) are influenced by shear stress and neighboring smooth muscle cells (SMCs). We investigated the inflammation-relevant gene expression in EC/SMC cocultures under static condition and in response to shear stress. Under static condition, DNA microarrays and reverse-transcription polymerase chain reaction identified 23 inflammation-relevant genes in ECs whose expression was significantly affected by coculture with SMCs, with 18 upregulated and 5 downregulated. Application of shear stress (12 dynes/Cm2) to the EC side of the coculture for 6 h inhibited most of the proinflammatory gene expressions in ECs induced by coculture with SMCs. Inhibition of nuclear factor-κB (NF-κB) activation by the p65-antisense, lactacystin, and N-acetyl-cysteine blocked the coculture-induced EC expression of proinflammatory genes, indicating that the NF-κB binding sites in the promoters of these genes play a significant role in their expression as a result of coculture with SMCs. Chromatin immunopptn. assays demonstrated the in vivo regulation of NF-κB recruitment to selected target promoters. Shear stress inhibited the SMC coculture-induced NF-κB activation in ECs and monocytic **THP-1** cell adhesion to ECs. Our findings suggest that shear stress plays an inhibitory role in the proinflammatory gene expression in ECs located in close proximity to SMCs.

L3 ANSWER 10 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN
2005:180429 Document No. 143:907 Kurarinone isolated from Sophora flavescens Ait inhibited **MCP-1**-induced chemotaxis. Lee, Seung Woong; Lee, Hyun Sun; Nam, Jung Yeon; Kwon, Oh Eok; Baek, Jin Ah; Chang, Jong Sun; Rho, Mun-Chual; Kim, Young Kook (Laboratory of Lipid Metabolism, Korea Research Institute of Bioscience and Biotechnology, Yusong-gu, Taejeon, 305-333, S. Korea). Journal of Ethnopharmacology, 97(3), 515-519 (English) 2005. CODEN: JOETD7. ISSN: 0378-8741. Publisher: Elsevier Ireland Ltd..
AB The accumulation of circulating monocytes in the arterial wall is an early in atherosclerotic plaque formation. Monocyte chemoattractant protein-1 ( **MCP-1**) promotes the migration of monocytes and would play a role in the development of atherosclerotic lesions. Searching for inhibitors of **MCP-1**-induced cell migration from natural sources, we isolated one active compound through active-guided fractionations from the MeOH exts. of Sophora flavescens Ait (Leguminosae). On the basis of spectral evidence, the structure of active compound was identified as kurarinone. It inhibited the migration of **THP-1** cells induced by **MCP-1** with IC50 value of 19.2 μg/mL. In addition, it inhibited the binding of **MCP-1** to **THP-1** cells and phosphorylation of p42/44 MARK.

L3 ANSWER 20 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN
2004:755741 Document No. 141:307283 Effects of benidipine, a

dihydropyridine- Ca2+ channel blocker, on expression of cytokine-induced adhesion molecules and chemoattractants in human aortic endothelial cells. Matsubara, Masahiro; Hasegawa, Kazuhide (Department of Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Nagaizumi-cho, Sunto-gun, Shizuoka, 411-8731, Japan). European Journal of Pharmacology, 498(1-3), 303-314 (English) 2004. CODEN: EJPHAZ. ISSN: 0014-2999. Publisher: Elsevier B.V..

AB Benidipine hydrochloride (benidipine) is a dihydropyridine-Ca2+ channel blocker with antioxidant properties. We examined the effects of benidipine on cytokine-induced expression of adhesion mols. and chemokines, which play important roles in the adhesion of monocytes to endothelium. Pretreatment of human aortic endothelial cells (HAECs) with benidipine (0.3 - 10 μmol/l) for 24 h significantly suppressed cytokine-induced vascular cell adhesion mol.-1 (VCAM-1) and intracellular cell adhesion mol.-1 (ICAM-1) mRNA and protein expression, resulting in reduced adhesion of **THP-1** monocytes. Benidipine also suppressed induction of monocyte chemoattractant protein (**MCP**)-**1** and interleukin-8. Benidipine inhibited redox-sensitive transcriptional nuclear factor-κB (NF-κB) pathway, as determined by Western blotting of inhibitory κB (IκB) phosphorylation and luciferase reporter assay. Results of anal. using optical isomers of benidipine and antioxidants suggested that these inhibitory effects were dependent on pharmacol. effects other than Ca2+ antagonism such as antioxidant effects. Benidipine may thus have anti-inflammatory properties and benefits for in the treatment of atherosclerosis.

L3 ANSWER 30 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

2004:422814 Document No. 141:223674 C-Reactive Protein Promotes Monocyte Chemoattractant Protein-1-Mediated Chemotaxis Through Upregulating CC Chemokine Receptor 2 Expression in Human Monocytes. Han, Ki Hoon; Hong, Kyung-Hee; Park, Jae-Hyeong; Ko, Jesang; Kang, Duk-Hyun; Choi, Kee-Joon; Hong, Myeong-Ki; Park, Seong-Wook; Park, Seung-Jung (Asan Medical Center, University of Ulsan College of Medicine, Seoul, S. Korea). Circulation, 109(21), 2566-2571 (English) 2004. CODEN: CIRCAZ. ISSN: 0009-7322. Publisher: Lippincott Williams & Wilkins.

AB Inflammation plays a crucial role in atherosclerosis. An elevated serum C-reactive protein (CRP) level is a strong marker for future atherosclerotic cardiovascular diseases. In addition, recent data suggest that CRP may directly promote atherogenesis. Here, the authors investigated investigated whether CRP can directly activate human circulating monocytes. Incubation of **THP-1** monocytes with CRP (10 μg/mL) increased CC chemokine receptor 2 (CCR2) expression at both the protein and transcript levels, which in turn enhanced chemotaxis mediated by monocyte chemoattractant protein-1 (**MCP-1**) up to 2-fold. The CRP-induced upregulation of CCR2 expression involved binding of CRP to the FcγR, most notably FcγRI, and phospholipase D1 activation. Serum high-sensitivity CRP levels in 52 normocholesterolemic human subjects were pos. correlated with CCR2 surface expression on circulating monocytes and **MCP-1**-mediated monocyte chemotaxis. Thus, elevated blood CRP levels may promote accumulation of monocytes in the atherogenic arterial wall by increasing chemotactic activities of monocytes in response to **MCP-1**

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L3 ANSWER 40 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

2003:586448 Document No. 140:22888 Dobutamine inhibits monocyte chemoattractant protein-1 production and chemotaxis in human monocytes. Li, Chi-Yuan; Tsai, Chien-Sung; Chueh, Sheau-Huei; Hsu, Ping-Ching; Wang, Jia-Yi; Wong, Chih-Shung; Ho, Shung-Tai (Department of Anesthesiology, Tri-Service General Hospital, Taipei, Taiwan, Peop. Rep. China). Anesthesia & Analgesia (Baltimore, MD, United States), 97(1), 205-209 (English) 2003. CODEN: AACRAT. ISSN: 0003-2999. Publisher: Lippincott Williams & Wilkins.

AB It has been reported that, in patients with acute myocardial infarction or

congestive heart failure, monocyte chemoattractant protein-1 (**MCP-1**) plays an important role in the development of inflammatory responses and that the level of **MCP-1** is correlated with the severity of the disease. We conducted this study to investigate the effects of dobutamine and dopamine on lipopolysaccharide (LPS)-induced **MCP-1** production in human monocytic **THP-1** cells. Monocytes were incubated in vitro with LPS for 16 h at 37°C in the presence or absence of dobutamine or dopamine. ELISA was used to examine the effect of dobutamine on **MCP-1** synthesis, with the **MCP-1** mRNA expression examined by reverse transcriptase-polymerase chain reaction. Dobutamine inhibited LPS-induced production of **MCP-1**, as well as mRNA expression, in a dose-dependent manner, whereas dopamine had no significant effect. Furthermore, we demonstrated that dobutamine suppressed **MCP-1**-induced chemotaxis and peak [Ca2+]i in monocytic **THP-1** cells. These findings suggest that dobutamine may modulate monocyte activation, such as chemotaxis and [Ca2+]i, as well as **MCP-1** production, during therapy for congestive heart failure.

L3 ANSWER 50 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

2002:857387 Document No. 138:284562 Nonrequirement of Continuous Stimulation with **MCP-1** for Cell Migration and Determination of Directional Migration by Initial Stimulation with Chemokine. Kito, Keiji; Nishida, Ken-ichi (New Product Research Laboratories II, Daiichi Pharmaceutical Company Ltd., Tokyo, 134-8630, Japan). Experimental Cell Research, 281(1), 157-166 (English) 2002. CODEN: ECREAL. ISSN: 0014-4827. Publisher: Elsevier Science.

AB Monocyte chemoattractant protein-1 (**MCP-1**) induces monocyte migration through interaction with the **MCP-1** receptor CCR2. In this report we have examined the length of chemokine stimulation necessary for induction of cell migration and whether continuous stimulation is required for active migration. Monocytic **THP-1** cells prestimulated with **MCP-1** for 15 to 30 min exhibited a migration response after the chemokine was removed from the culture medium, indicating that a short exposure to chemokine stimulation is sufficient for migration of **THP-1** cells and continuous stimulation is not required for active migration. A reverse gradient of **MCP-1** had no effect on migration after prestimulation with **MCP-1**. This implies that cells are determined to directionally migrate by initial stimulation with **MCP-1**. Furthermore, cell migration after prestimulation with **MCP-1** was inhibited by a p38 inhibitor, but not by a phosphatidylinositol 3-kinase (PI3-kinase) inhibitor, indicating that p38, but not PI3-kinase, is involved in the migration response after the determination of direction by initial chemokine stimulation.

L3 ANSWER 60 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

2002:82983 Document No. 136:277167 Secretory phospholipase A2 elicits proinflammatory changes and upregulates the surface expression of Fas ligand in monocytic cells. Potential relevance for atherogenesis. Hernandez, Marita; Fuentes, Lucia; Aviles, Francisco Javier Fernandez; Crespo, Mariano Sanchez; Nieto, Maria Luisa (Instituto de Biologia Genetica Molecular, Facultad de Medicina, Hospital Clinico Universitario, Valladolid, Spain). Circulation Research, 90(1), 38-45 (English) 2002. CODEN: CIRUAL. ISSN: 0009-7330. Publisher: Lippincott Williams & Wilkins.

AB Type I1A secretory phospholipase A2 (sPLA2) is an acute-phase reactant that plays a role in atherogenesis and is expressed in atherosclerotic arterial walls displaying inflammatory features. This generates a relevant question addressing the biol. effects of this enzyme on monocytic cells, in view of the role of these cells in the inflammatory process associated with atherosclerosis. SPLA2 produced a mild activation of the p42

mitogen-activated protein module of the mitogen-activated protein kinase (MAPK) cascade and a prominent activation of c-Jun N-terminal kinase in **THP-1** monocytes. This activation showed both an early and a late peak. different from that elicited by tumor necrosis factor-α (TNF-α), which only showed the first peak. This was accompanied by activation of arachidonate metabolism, as judged from both the activation of the cytosolic phospholipase A2 (cPLA2) and the induction of cyclooxygenase-2 (COX-2) expression. SPLA2 also elicited the production of monocyte chemoattractant protein-1 (**MCP-1**) and showed a synergistic effect with TNF-α on both COX-2 induction and **MCP-1** production· SPLA2 upregulated the expression of Fas ligand at the cell surface, but it did not influence Fas expression nor cell survival of monocytes. In summary, these data indicate that some of the atherogenic effects of sPLA2 can be exerted by engagement of an sPLA2-binding structure on monocytic cells, most probably the M-type receptor for sPLA2, which produces the activation of the MAPK cascade, induces a proinflammatory phenotype, and upregulates the cell surface expression of Fas ligand.

L3 ANSWER 70 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN
2001:527088 Document No. 135:240732 Homocysteine stimulates the expression of monocyte chemoattractant protein-1 receptor (CCR2) in human monocytes: possible involvement of oxygen free radicals. Wang, Guoping; Karmin, O. (Department of Pharmacology, Institute of Cardiovascular Science and Medicine, Faculty of Medicine, University of Hong Kong, Hong Kong, Peop. Rep. China). Biochemical Journal, 357(1), 233-240 (English) 2001. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press Ltd..
AB Homocysteinemia is an independent risk factor for atherosclerosis. The development of atherosclerosis involves monocyte chemoattractant protein 1 (**MCP-1**)-mediated monocyte recruitment to the lesion site. The action of **MCP-1** is mostly via its interaction with **MCP-1** receptor (CCR2), which is the major receptor for **MCP-1** on the surface of monocytes. The objective of the present study was to investigate the effect of homocysteine on CCR2 expression in human **THP-1** monocytes. Cells were incubated with various concns. of homocysteine for 6, 12, 24 and 48 h. The expression of CCR2 mRNA was determined by nuclease protection assay and the CCR2 protein was measured by Western immunoblotting anal. The binding of **MCP-1** to CCR2 as a functional receptor on the monocyte surface was determined by flow cytometry. Homocysteine (0.05-0.2 mM) significantly enhanced the expression of CCR2 mRNA (129-209% of the control) and CCR2 protein (up to 183% of control) in these cells after 24 h of incubation. Stimulation of CCR2 expression was associated with a parallel increase in the binding activity of CCR2 (129-191% of control) as well as an enhanced chemotactic response of homocysteine-treated monocytes. Further investigation revealed that the levels of superoxide were significantly elevated in cells incubated with homocysteine for 12-48 h. The addition of superoxide dismutase, a scavenger of superoxide, to the culture medium abolished the stimulatory effect of homocysteine on CCR2 expression as well as the binding activity of the receptor. The stimulatory effect of homocysteine on the expression of CCR2 mRNA and the levels of CCR2 protein was also observed in human peripheral blood monocytes. In conclusion, the present study has clearly demonstrated that homocysteine stimulates CCR2 expression in monocytes, leading to an enhanced binding activity and chemotactic response. Homocysteine-induced superoxide formation might serve as one of the underlying mechanisms for this effect.

L3 ANSWER 80 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN
2001:266676 Document No. 135:32597 Amyloid-β peptide fragments p3 and p4 induce pro-inflammatory cytokine and chemokine production in vitro and in vivo. Szczepanik, Ann Marie; Rampe, David; Ringheim, Garth E. (Department of CNS, Aventis Pharmaceuticals, Inc., Bridgewater, NJ, 08807-0800, USA). Journal of Neurochemistry, 77(1), 304-317 (English)

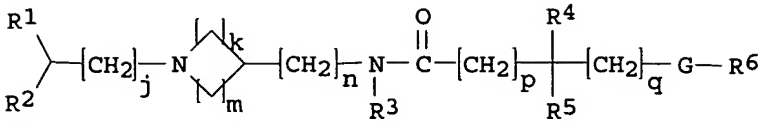
2001. CODEN: JONRA9. ISSN: 0022-3042. Publisher: Blackwell Science Ltd..

AB Alzheimer's disease (AD) pathol. is characterized by senile plaques containing amyloid-β (Aβ) peptide, a protein with neurotoxic and glial immune activating potential. In addition to the highly amyloidogenic peptides Aβ(1-40/42), plaques contain amino-terminal truncated Aβ peptides including the alpha secretase-generated p3 fragments Aβ(17-40/42). In the present study, Aβ(17-40/42), Aβ(1-40/42), Aβ(1-16), and Aβ(25-35) aged in different solvents exhibited varying capacity to activate the murine microglia cell line MG-7 depending on solvent, peptide "aging", and peptide sequence that did not strictly correlate with β-sheet formation. Aβ(17-40/42) or Aβ(1-42) stimulated production of the pro-inflammatory cytokines interleukin (IL)-1α, IL-1β, IL-6 and tumor necrosis factor-α (TNF-α), and the chemokine **MCP-1** from differentiated human monocytes (**THP-1**) while little or no stimulation was observed with the other Aβ fragments. MG7 cells also produced these five pro-inflammatory proteins in response to Aβ(1-42), whereas Aβ(17-40/42) elicited mainly TNF-α and **MCP-1**. Murine and human astrocyte cell lines (D30 and U373, resp.) were generally less responsive to Aβ fragments producing mainly IL-6 and **MCP-1** in response to Aβ(1-42) or Aβ(17-40/42) fragments. In mice, an intracerebroventricular infusion of Aβ(1-42) significantly increased IL-1α, IL-1β, IL-6 and **MCP-1** while Aβ(17-40/42) increased **MCP-1** and Aβ(17-40) increased IL-1β. These results demonstrate that p3 and p4 Aβ fragments are pro-inflammatory glial modulators and thus may play a role in development of the immunopathol. observed in AD.

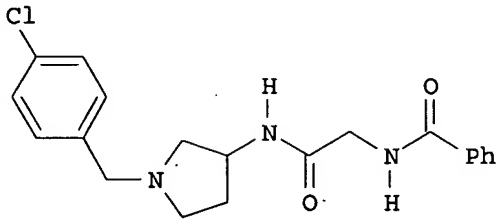
L3 ANSWER 100 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

1999:350650 Document No. 131:18925 Preparation of cyclic amine derivatives for inhibition of the action of chemokines such as MIP-1α and/or MCP-1 on target cells. Shiota, Tatsuki; Kataoka, Kenichiro; Imai, Minoru; Tsutsumi, Takaharu; Sudoh, Masaki; Sogawa, Ryo; Morita, Takuya; Hada, Takahiko; Muroga, Yumiko; Takenouchi, Osami; Furuya, Monoru; Endo, Noriaki; Tarby, Christine M.; Moree, Wil A.; Teig, Steven L. (Teijin Ltd., Japan; Combichem, Inc.). PCT Int. Appl. WO 9925686 A1 19990527, 374 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US23254 19981117. PRIORITY: US 1997-972484 19971118; US 1998-55285 19980813; US 1998-133434 19980813.

GI



I



II

AB The title compds. [I; R1 = (un)substituted Ph, cycloalkyl, heteroaryl, etc.; R2 = H, alkyl, alkoxycarbonyl, etc.; j = 0-2; k = 0-2; m = 2-4; n = 0-1; R3 = H, alkyl; R4, R5 = H, OH< Ph, etc.; p = 0-1; q = 0-1; G = CO, SO, CO2, etc.; R6 = Ph, cycloalkyl, cycloalkenyl, etc.] and their pharmaceutically acceptable acid addition salts which inhibit the action of chemokines such as MIP-1α and/or MCP-1 on target cells and may be useful as a therapeutic drug and/or preventative drug in diseases, such as atherosclerosis, rheumatoid arthritis, and the like where blood monocytes and lymphocytes infiltrate into tissues, were prepared Thus, reaction of N-benzoylglycine with 3-amino-1-(4-chlorobenzyl)pyrrolidine.2HCl in the presence of 3-ethyl-1-[3-(dimethylaminopropyl)]carbodiimide.HCl, 1-hydroxybenzotriazole and Et3N in CHCl3 afforded 95% II which showed 50-80% inhibition of MIP-1α binding to THP-1 cells at 10 μM.

L3 ANSWER 120 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN

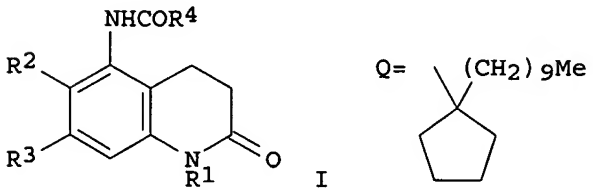
1996:562149 Document No. 125:219222 I-309/T cell activation gene-3 chemokine protects murine T cell lymphomas against dexamethasone-induced apoptosis. Van Snick, Jacques; Houssiau, Frederic; Proost, Paul; Van Damme, Jo; Renauld, Jean-Christophe (Ludwig Institute for Cancer Research, University of Louvain, Brussels, Belg.). Journal of Immunology, 157(6), 2570-2576 (English) 1996. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB We have previously reported that cytokines such as IL-9, IL-4, and IL-6 protect murine thymic lymphoma cell lines against dexamethasone-induced apoptosis. A similar activity, which could not be ascribed to any of these factors, was found in a number of human T cell supernatants that enabled mouse BW5147 thymic lymphoma not only to escape apoptosis but also to maintain proliferation. The protein responsible for this activity was purified to homogeneity from the culture medium of activated leukemic T cells and was found to be identical with the I-309 chemokine. Half-maximal anti-apoptotic activity was obtained with .apprx.1 ng/mL, a concentration considerably lower than that required for the monocyte chemotactic activity of this mol., as measured on **THP-1** cells. The purified I-309 also improved the survival of two other mouse thymic lymphoma cell lines. This activity was as potent as that of IL-9, which was the strongest anti-apoptotic factor found to date for these cells. Similar results were obtained for BW5147 cells with recombinant I-309 and with T cell activation gene-3, the murine homolog of I-309, but not with other members of the chemokine family, including IL-8, neutrophil-activating peptide-2, granulocyte chemotactic protein-2, macrophage inflammatory protein-1a, RANTES (regulated upon activation, normal T cell expressed and secreted), monocyte chemotactic protein-1 ( **MCP-1**), and MCP-2. MCP-3, however, showed a minor, but significant effect in this model. Unlike that of IL-9, the activity of

I-309 was completely inhibited in the presence of pertussis toxin, indicating the involvement of a G protein in this process.

L3 ANSWER 130 OF 140 CAPLUS COPYRIGHT 2005 ACS on STN
1995:563278 Document No. 122:314466 Preparation of 5-acylamino-2-quinolone derivative as acyl-CoA:cholesterol acyltransferase (ACAT). Shioda, Tatsuki; Kataoka, Kenichiro; Mochizuki, Tsutomu; Endo, Noriaki (Teijin Ltd, Japan). Jpn. Kokai Tokkyo Koho JP 07002782 A2 19950106 Heisei, 9 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1993-144944 19930616.

GI




AB The title compound [I; R1 = H, (un)substituted C1-3 alkyl or acyl; R2, R3 = (un)substituted C1-3 alkyl; R4 = (un)substituted C6-10 aryl, C3-20 cycloalkyl or alkenyl optionally substituted at a position other than 1-position, CR5R6R7; wherein R5, R6 = H, (un)substituted C1-6 alkyl or R5 and R6 together form a C3-7 carbocyclic ring; R7 = H, (un)substituted C1-20 alkyl, C2-20 alkenyl, C6-10 aryl, or C7-20 aralkyl] and a pharmacol. acceptable salt thereof, which also inhibit the production of monocyte chemotactic protein-1 (**MCP-1**) and are useful as a hypolipidemic, antiarteriosclerotic, and antiinflammatory agent, are prepared Thus, 92 mg 1-decylcyclopentanecarbonyl chloride was added to a solution of 43 mg 5-amino-1,6,7-trimethyl-1,2,3,4-tetrahydroquinolin-2-one (preparation given) and 33 mg Et3N in 2 mL CH2Cl2 and the mixture was stirred at room temperature for 5 h to give, after silica gel chromatog., 64 mg title compound I (R1 = R2 = R3 = Me, R4 = Q) (II). II in vitro showed IC50 of 4.2 + 10-7 M against ACAT preparation from microsomes of mucus membrane of a rabbit small intestine. It also dose-dependently inhibited the production ( **MCP-1** gene expression) of **MCP-1** in human monocytic leukemia **THP-1** cells.

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1993:145745 Document No. 118:145745 Characterization and species distribution of high affinity GTP-coupled receptors for human Rantes and monocyte chemoattractant protein 1. Van Riper, Gail; Siciliano, Salvatore; Fischer, Paul A.; Meurer, Roger; Springer, Martin S.; Rosen, Hugh (Dep. Biochem., Merck Res. Lab., Rahway, NJ, 07065, USA). Journal of Experimental Medicine, 177(3), 851-6 (English) 1993. CODEN: JEMEAV. ISSN: 0022-1007.

AB Equilibrium binding studies with recombinant human chemoattractant cytokines Rantes and monocyte chemoattractant protein 1 (**MCP-1**) on monocytic **THP-1** cells have allowed the functional identification of two distinct receptors for C-C chemokines. One is a novel oligospecific receptor with high affinity for Rantes (50% maximal inhibitory concentration [IC50], 0.68 nM) and low affinity (IC50, 35 nM) for **MCP-1**, while the other is the previously described specific receptor for **MCP-1** (IC50, 0.5 nM). Receptor affinity for Rantes is enhanced on preparation of isolated membranes with a 12-fold decrease in receptor Kd. The basis of this enhancement is not understood. The Rantes receptor appears to be G protein linked, as binding activity is abolished by guanosine 5'-O-(3-thiotriphosphate) (IC50, 7.3 nM). In contrast to the consequences of **MCP-1** binding, no ligand-dependent calcium fluxes were demonstrated on

binding of Rantes to human monocytes or THP-1 cells. The binding of Rantes and MCP-1 to mononuclear cells from dog, rabbit, and rat were tested. While high affinity binding could be demonstrated in dog and rabbit, differences in ligand-induced Ca2+ fluxes could be shown between species. This suggests that receptor-ligand interactions and receptor coupling is best examined with autologous receptors and cytokine.

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